AMENDMENTS TO THE SPECIFICATION

In the application:

Please add to the application the Sequence Listing containing 58 pages submitted under 37 C.F.R. §§1.821-1.825.

In the specification:

Please replace paragraph [0051], beginning on page 13 with the following paragraph:

--For example, a native synthesized BoNT/A can comprise: MPFVNKQFNYKD, (SEQ ID NO:123) whereas a native processed BoNT/A can comprise PFVNNQFNYKD (SEQ ID NO:124). Thus a proposed 8 amino acid deletion would retain the YKD amino acid residues, while a recombinantly produced deletion would retain the MYKD (SEQ ID NO:125) amino acid residues.--

Please replace paragraph [00113], beginning on page 26 with the following paragraph:

--In one embodiment, the leucine-based motif is xDxxxLL, (SEQ ID NO:126) wherein x can be any amino acids. In some embodiments, the leucine-based motif is xExxxLL, (SEQ ID NO:127) wherein E is glutamic acid. In some embodiments, the duplet of amino acids can include an isoleucine or a methionine, forming xDxxxLI (SEQ ID NO:128) or xDxxxLM, (SEQ ID NO:129) respectively. Additionally, the aspartic acid, D, can be replaced by a glutamic acid, E, to form xExxxLI, (SEQ ID NO:130) xExxxIL (SEQ ID NO:131) and xExxxLM (SEQ ID NO:132). In a suitable embodiment, the leucine-based motif is phenylalanine-glutamate-phenylalanine-tyrosine-lysine-leucine-leucine, SEQ ID NO:1.--

Please replace paragraph [00140], beginning on page 34 with the following paragraph:

--Tyrosine-based motifs are within the scope of the present invention as biological persistence and/or a biological activity altering components. Tyrosine-based motifs comprise the sequence Y-X-X-Hy (SEQ ID NO:133) where Y is tyrosine, X is any amino acid and Hy is a

hydrophobic amino acid. Tyrosine-based motifs can act in a manner that is similar to that of leucine-based motifs. In Fig. 3 some of tyrosine motifs found in the type A toxin light chain are bracketed. In addition, a tyrosine-based motif is found within the leucine-based motif which is indicated by an asterisked bracket in Fig. 3.--

Please replace paragraph [00143], beginning on page 34 with the following paragraph:

--Fig. 8 shows a sequence alignment between type A and type B light chains isolated from strains type A HallA (SEQ ID NO:24 and SEQ ID NO:25) and type B Danish I (SEQ ID NO:26 and SEQ ID NO:27) respectively. Light chains or heavy chains isolated from other strains of botulinum toxin types A and B can also be used for sequence comparison. The shaded amino acids represent amino acid identities, or matches, between the chains. Each of the shaded amino acids between amino acid position 10 and amino acid position 425 of the Fig. 8 consensus sequence, alone or in combination with any other shaded amino acid or amino acids, represents a biological persistence altering component that is within the scope of the present invention. For example, amino acids KAFK at positions 19 to 22, LNK at positions 304 to 306, L at position 228 in combination with KL at positions 95 and 96, FDKLYK at positions 346 to 351, YL-T at positions 78 to 81, YYD at positions 73 to 75 in combination with YL at positions 78 and 79 in combination with T a position 81, F at position 297 in combination with I at position 300 in combination with KL at positions 95 and 96 can be biological persistence altering components for use within the scope of this invention. In addition, conserved regions of charge, hydrophobicity, hydro-philicity and/or conserved secondary, tertiary, or quaternary structures that may be independent of conserved sequence are within the scope of the present invention.--

Please replace paragraph [00275], beginning on page 64 with the following paragraph:

--Additional studies showed that a GFP-LCA construct with eight amino acid residues (PFVNKQFN) (SEQ ID NO:135) deleted from the N-terminus (no C-terminus deletion) localized in PC12 cells a very similar pattern to the localization in PC12 cells of a truncated GFP-LCA construct with both the C and N terminus deletions.--

Please replace paragraph [00276], beginning on page 64 with the following paragraph:

--Further studies showed that a GFP-LCA construct with twenty two amino acid residues (KNFTG LFEFYKLLCV RGIITSK) (SEQ ID NO:136) deleted from the C-terminus (no N-terminus deletion) localized in PC12 cells in a very similar manner to that of the GFP-LCA(LL-->AA) mutant.--

Please replace paragraph [00277], beginning on page 64 with the following paragraph:

--A GFP-LCA construct with both eight amino acid residues (PFVNKQFN) (SEQ ID NO:135) deleted from the N-terminus and twenty two amino acid residues (KNFTG LFEFYKLLCV RGIITSK) (SEQ ID NO:136) deleted from the C-terminus accumulated intracellularly.--

Please replace paragraph [00278], beginning on page 65 with the following paragraph:

--The first 30 residues of the amino-terminus (N-term) and the last 50 residues of the carboxyl-terminal (C-term) of the amino acid sequences of botulinum toxin serotypes A through G light chains (LC) are shown in Table 2.

Table 2

toxin	N-term (AAs 1-30) of LC	C-term (last 50 AAs) of LC	Seq ID #
BoNT/A	MPFVNKQFNYKDPVN GVDIAYIKIPNAGQM	GFNLRNTNLAANFNGQNTEINNMNF TKLKNFTGLFEFYKLLCVRGIITSK	14/15
BoNT/B	MPVTINNFNYNDPIDN DNIIMMEPPFARGT	YTIEEGFNISDKNMGKEYRGQNKAI NKQAYEEISKEHLAVYKIQMCKSVK	16/17
BoNT/C1	MPITINNFNYSDPVDN KNILYLDTHLNTLA	NIPKSNLNVLFMGQNLSRNPALRKV NPENMLYLFTKFCHKAIDGRSLYNK	18/19
BoNT/D	MTWPVKDFNYSDPVN DNDILYLRIPQNKLI	YTIRDGFNLTNKGFNIENSGQNIERN PALQKLSSESVVDLFTKVCLRLTK	20/21
BoNT/E	MPKINSFNYNDPVNDR TILYIKPGGCQEFY	GYNINNLKVNFRGQNANLNPRIITPIT GRGLVKKIIRFCKNIVSVKGIRK	22/23
BoNT/F	MPVAINSFNYNDPVN DDTILYMQIPYEEKS	TVSEGFNIGNLAVNNRGQSIKLNPKII DSIPDKGLVEKIVKFCKSVIPRK	24/25
BoNT/G	MPVNIKXFNYNDPINN DDIIMMEPFNDPGP	QNEGFNIASKNLKTEFNGQNKAVNK EAYEEISLEHLVIYRIAMCKPVMYK	26/27--

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Please replace paragraph [00280], beginning on page 65 with the following paragraph:

--Examples of amino acid sequence substitutions include the replacement of one or more contiguous or non-contiguous amino acids in the first 30 amino acids of the N-terminus and/or the last 50 amino acids of the C-terminus of the light chain with an equal number and placement of amino acids that differ from the wild-type sequence. Substitutions can be conservative or non-conservative of the character of the amino acid. For example, the amino acid valine at a specific position in the wild-type sequence can be replaced with an alanine in the same position in the substituted sequence. Furthermore, basic residues such as arginine or lysine can be substituted for highly hydrophobic residues such as tryptophan. A proline or histidine residue may be substituted in order to form or disrupt a potentially important structural or catalytic element of the protein. Some examples of amino acid substitutions are indicated by bold underlined text in the sequences described in Table 3.

Table 3

toxin	N-term (AAs 1-30) of LC	C-term (last 50 AAs) of LC	Seq ID #
BoNT/A	MPF**A**NKQFNYKDPVN GVDIAYIKIPNAGQM	GFNLRNTNLAANFNGQNTEINNM N**R**TKLKNFTGLFEFYKLLCVRGIIT SK	28/29
BoNT/A	MPFVNKQFN**K**KDPVN GVDIAYIKIPNAGQM	GFNLRNTNLAANFNGQNTEINNM NFTKLKN**AA**GLFEFYKLLCVRGIIT SK	30/31
BoNT/A	MPFVNKQFNYKDPVN GVDIA**R**IKIPNAGQM	GFNLRNTNLAAN**H**NGQNTEINNM NFTKLKNFTGLFEFYKLLCVRGIIT SK	32/33
BoNT/A	MPFVNK**H**FNYKDPVN GVDIAYIKIPNAGQM	GFNLRNTNLAANFNGQNTEINNM NFTKLKNFTGLFEFYKLLC**A**RGIIT SK	34/35
BoNT/B	MP**A**TINNFNYNDPIDN DNIIMMEPPFARGT	YTIEEGFNISDKNMGKEYRGQNKA INKQAYEEISKEHLAVYKI**R**MCKS VK	36/37
BoNT/B	MPVTINNFNYNDPIDN DNII**AA**EPPFARGT	YTIEEGFNISDKNMGKEYRGQNKA INKQAYEEISKEHLAV**R**KIQMCKS VK	38/39
BoNT/B	MPVTINNFN**R**NDPIDN DNIIMMEPPFARGT	YTIEEGFNISDKNMGKEYRGQNKA INKQA**K**EEISKEHLAVYKIQMCKS VK	40/41
BoNT/C1	MPITINN**K**NYSDPVDN KNILYLDTHLNTLA	NIPKSNLNVLFMGQNLSRNPALRK VNPENMLYLFTKFCHKAIDGRSL**R**	42/43

		NK	
BoNT/D	MTWPAKDFNYSDPAN DNDILYLRIPQNKLI	YTIRDGFNLTNKGFNIENSGQNIER NPALQKLSSESVVDLFTKACLRLT K	44/45
BoNT/E	MPKINSFNYNDPANDR TILYIKPGGCQEFY	GYNINNLKVNFRGQNANLNPRIITP ITGRGHVKKIIRFCKNIVSVKGIRK	46/47
BoNT/E	MPKINSRNYNDPVND RTILYIKPGGCQEFY	GYNINNLKVNFRGQNANLNPRIITP ITGRGLVKKIIRFCKNAASVKGIRK	48/49
BoNT/E	MPKINSFNYNDPVNDR TILYIKPGGCQEFR	GYNINNLKVNFRGQNANLNPRIITP ITGRGLVKKIIRFCKNIVSAKGIRK	50/51
BoNT/F	MPAAINSFNYNDPVN DDTILYMQIPYEEKS	TVSEGFNIGNLAVNNRGQSIKLNP KIIDSIPDKGLVEKIVKFCKSAIPRK	52/53
BoNT/G	MPVNIKXHNYNDPIN NDDIIMMEPFNDPGP	QNEGFNIASKNLKTEFNGQNKAVN KEAYEEISLEHLVIYRIAMCKPAM YK	54/55--

Please replace paragraph [00281], beginning on page 67 with the following paragraph:

--Examples of amino acid sequence mutations include changes in the first 30 amino acids of the N-terminus and/or the last 50 amino acids of the C-terminus of the light chain sequence such that one or several amino acids are added, substituted and/or deleted such that the identity, number and position of amino acids in the wild-type light chain sequence is not necessarily conserved in the mutated light chain sequence. Some examples of amino acid sequence mutations are described in Table 4, in which additions of amino acids are shown in bold underlined text, and deletions are indicated by dashes in the sequences shown.

Table 4

toxin	**N-term (AAs 1-30) of LC**	**C-term (last 50 AAs) of LC**	**Seq ID #**
BoNT/A	MPFVNKQFNYKDPVN GVDIAYIKIPH----	GFNLRNTNLAANFNGQNTEINNM NAAAAAAAAAA-------CVRGIITSK	56/57
BoNT/A	MAAA---- NYKDPVNGVDIAYIKI PNAGQM	GKNLRNTNLAANFNGQNTEINNM NFTKLKNFTGLFEFYK— CVRGIITSK	58/59
BoNT/A	MPFVNKQFNYKDPVN GVDIAR----NAGQM	GFNLRNTNLAA---- HNTEINNMNFTKLKNFTGLFEFYK LLCVRGIITSK	60/61

BoNT/A	MPKVNKQFN---- VNGVDIAYIKIPNAGQ M	GFNLRNTNLAANFNGQNTEINNM NFTKLKNFTGLFEFRR--------TSK	62/63
BoNT/B	MPVTINNFNYNDPIDN DNIIAAAAAAARGT	YTIPPGFNISDKNMGKEYRGQNKA INKQAYEEISKEH----------	64/65
BoNT/B	MPA---- FNYNDPIDNDNIIMME PPFARGT	YTIEEGFNISDKNMGKEYRGQNKA AAAAAAEEISKEHLAVYKIQMCKS VK	66/67
BoNT/B	MPVTINNFNR---------- MMEPPFARGT	YTIEEGFNISDKNMGKEYRGQNKA INKQAY------AAAAAAIQMCKSVK	68/69
BoNT/C1	M--------- SDPVDNKNILYLDTHL NTLA	NIPKSNLNVLFMGQNLSRNPALRK VNPENMLAAA--- CHKAIDGRSLYNK	70/71
BoNT/D	MTRPVKD---- DPVNDNDILYLRIPQN KLI	YTIRDGFNLTNKGFNIENSGQNIER NPALQKL------DLPPKVCLRLTK	72/73
BoNT/E	MPKINSPPNYNDPVND RTILYIKPGGCQEFY	GYNINNLKVNFRGQNANLNPRIITP ITGRGLVKKAAAACKNIVSVKGIR K	74/75
BoNT/E	MPKINSFNYNDPAAA ANDRTILYIKPGGCQE FY	GYNINNLKVNFRGQNANLNPRIITP ITGRGLV---HRFCKNIVSVKGIRK	76/77
BoNT/E	MPKINSFNYNDPVNDR TILKIKPGGCKEFY	GYNINNLKVNFRGQNANLNPRIITP ITGRGLPP----------	78/79
BoNT/F	MP------ NYNDPVNDDTILYMQI PYEEKS	TVSEGFNIGNLAVNNRGQSIKLNP KIIDSIPDKGAAAAAA--CKSVIPRK	80/81
BoNT/G	MPVNIPP---- DPINNDDIIMMEPFND PGP	QNEGFNIASKNLKTEFNGQNKAVN KEAY----------AAAAAAA	82/83--

Please replace paragraph [00282], beginning on page 68 with the following paragraph:

--Examples of amino acid sequence deletions include the removal of one or more contiguous or non-contiguous amino acids from the first 30 amino acids of the N-terminus and/or the last 50 amino acids of the C-terminus of the light chain sequence. Some examples of amino acid sequence deletions are indicated by dashes in the sequences shown in Table 5.

Table 5

toxin	**N-term (AAs 1-30) of LC**	**C-term (last 50 AAs) of LC**	**Seq ID #**
BoNT/A	M-------- YKDPVNGVDIAYIKIP	GFNLRNTNLAANFNGQNTEINNMNFT	84/85

	NAGQM	KLKNFTGLFEFYK----------	
BoNT/A	MPFVNKQ------ VNGVDIAYIKIPNAGQ M	GFNLRNTNLAANFNGQNTEINNMNFT KLK----------LLCVRGIITSK	86/87
BoNT/A	MPFVNKQFNYKDP----- -AYIKIPNAGQM	GFNLRNTNLAANFNGQNTEINNMN---- ----GLFEFYKLLCVRGIITSK	88/89
BoNT/A	MPFVNKQFNYKDPVN GVDIA----------	GFNLRN---------- NTEINNMNFTKLKNFTGLFEFYKLLCV RGIITSK	90/91
BoNT/B	MPVTINNFNYNDPIDN DNIIMME-------	YTI----- ISDKNMGKEYRGQNKAINKQAYEEISK EHLAVYKIQMCKSVK	92/93
BoNT/B	MPVTINNFNYND------- ---EPPFARGT	YTIEEGFNISD-------- GQNKAINKQAYEEISKEHLAVYKIQM CKSVK	94/95
BoNT/B	MP-------- NDPIDNDNIIMMEPPF ARGT	YTIEEGFNISDKNMGKEYRGQNKAINK QA----------KIQMCKSVK	96/97
BoNT/C1	MPI------- SDPVDNKNILYLDTHL NTLA	NIPKSNLNVLFMGQNLSRNPALRKV---- ------KFCHKAIDGRSLYNK	98/99
BoNT/D	MTW---------- VNDNDILYLRIPQNKLI	YTIRDGFNLTNKGFNIENSGQNIERNPA ----------DLFTKVCLRLTK	100/101
BoNT/E	MP-------- DPVNDRTILYIKPGGC QEFY	GYNINNLKVNFRGQNANLNPRIITPI---- ------RFCKNIVSVKGIRK	102/103
BoNT/E	MPKINSFNYN---------- IKPGGCQEFY	GYNINN------ GQNANLNPRIITPITGRGLVKKIIRFCK NIVSVKGIRK	104/105
BoNT/E	MPKINSFNYNDPVNDR TILYIK--------	GYNINNLKVNFRGQNANLNPRIITPITG RGLVKKIIR--------KGIRK	106/107
BoNT/F	MPVAINSFNYNDPVN DDTILYMQIP-----	TVSEGFNIGNLAVNNRGQSIKLNPKIID SIPD--------KFCKSVIPRK	108/109
BoNT/G	M----------	QNEGFNIASKNLKTEFNGQNKAVNKE A----------RIAMCKPVMYK	110--

Please replace paragraph [00289], beginning on page 71 with the following paragraph:

--A chimeric botulinum toxin can be constructed such that a C-terminal portion of the light chain of one botulinum toxin serotype replaces a similar C-terminal portion within the light chain of another botulinum toxin serotype. For example, the last twenty two amino acid residues bearing the dileucine motif from the C-terminus of the light chain of BoNT/A can replace the last

twenty two amino acid residues of the C-terminus of the light chain of BoNT/E. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPKINSFNYNDPVNDRTILYIKPGGCQEFYKSFNIMKNIWIIPERNVIGTTPQDFHPPTSLKN
GDSSYYDPNYLQSDEEKDRFLKIVTKIFNRINNNLSGGILLEELSKANPYLGNDNTPDNQFH
IGDASAVEIKFSNGSQDILLPNVIIMGAEPDLFETNSSNISLRNNYMPSNHGFGSIAIVTFSPE
YSFRFNDNSMNEFIQDPALTLMHELIHSLHGLYGAKGITTKYTITQKQNPLITNIRGTNIEEF
LTFGGTDLNIITSAQSNDIYTNLLADYKKIASKLSKVQVSNPLLNPYKDVFEAKYGLDKDA
SGIYSVNINKFNDIFKKLYSFTEFDLATKFQVKCRQTYIGQYKYFKLSNLLNDSIYNISEGYN
INNLKVNFRGQNANLNPRIITPITG**KNFTGLFEFYKLLCVRGIITSK** (SEQ
ID NO:111)--

Please replace paragraph [00291], beginning on page 72 with the following paragraph:

--In a further example, the first thirty amino acid residues from the N-terminus of the light chain of BoNT/A can replace the first thirty amino acid residues of the N-terminus of the light chain of BoNT/B. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPFVNKQFNYKDPVNGVDIAYIKIPNAGQMGRYYKAFKITDRIWIIPERYTFGYKPEDFN
KSSGIFNRDVCEYYDPDYLNTNDKKNIFFQTLIKLFNRIKSKPLGEKLLEMIINGIPYLGDRR
VPLEEFNTNIASVTVNKLISNPGEVERKKGIFANLIIFGPGPVLNENETIDIGIQNHFASREGF
GGIMQMKFCPEYVSVFNNVQENKGASIFNRRGYFSDPALILMHELIHVLHGLYGIKVDDLP
IVPNEKKFFMQSTDTIQAEELYTFGGQDPSIISPSTDKSIYDKVLQNFRGIVDRLNKVLVCIS
DPNININIYKNKFKDKYKFVEDSEGKYSIDVESFNKLYKSLMLGFTEINIAENYKIKTRASYF
SDSLPPVKIKNLLDNEIYTIEEGFNISDKNMGKEYRGQNKAINKQAYEEISKEHLAVYKIQM
CKSVK (SEQ ID NO:112)--

Please replace paragraph [00293], beginning on page 72 with the following paragraph:

--Still further, the chimeric construct can have both N-terminal and the C-terminal replacements. For example, the first nine amino acid residues from the N-terminus of the light chain of BoNT/A can replace the first nine amino acid residues of the N-terminus of the light chain of BoNT/E. Additionally, in the same construct, the last twenty-two amino acid residues from the C-terminus of the light chain of BoNT/A can replace the last twenty-two amino acid residues from the C-terminus of the light chain of BoNT/E. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPFVNKQFNNDPVNDRTILYIKPGGCQEFYKSFNIMKNIWIIPERNVIGTTPQDFHPPTSLK
NGDSSYYDPNYLQSDEEKDRFLKIVTKIFNRINNNLSGGILLEELSKANPYLGNDNTPDNQF

HIGDASAVEIKFSNGSQDILLPNVIIMGAEPDLFETNSSNISLRNNYMPSNHGFGSIAIVTFSP
EYSFRFNDNSMNEFIQDPALTLMHELIHSLHGLYGAKGITTKYTITQKQNPLITNIRGTNIEE
FLTFGGTDLNIITSAQSNDIYTNLLADYKKIASKLSKVQVSNPLLNPYKDVFEAKYGLDKD
ASGIYSVNINKFNDIFKKLYSFTEFDLATKFQVKCRQTYIGQYKYFKLSNLLNDSIYNISEGY
NINNLKVNFRGQNANLNPRIITPITG**KNFTGLFEFYKLLCVRGIITSK** (SEQ
ID NO:113)--

Please replace paragraph [00295], beginning on page 73 with the following paragraph:

--Similarly, the first nine amino acid residues from the N-terminus of the light chain of BoNT/A can replace the first nine amino acid residues of the N-terminus of the light chain of BoNT/B. Additionally, in the same construct, the last twenty-two amino acid residues from the C-terminus of the light chain of BoNT/A can replace the last twenty-two amino acid residues from the C-terminus of the light chain of BoNT/B. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPFVNKQFNYNDPIDNDNIIMMEPPFARGTGRYYKAFKITDRIWIIPERYTFGYKPEDFNK
SSGIFNRDVCEYYDPDYLNTNDKKNIFFQTLIKLFNRIKSKPLGEKLLEMIINGIPYLGDRRV
PLEEFNTNIASVTVNKLISNPGEVERKKGIFANLIIFGPGPVLNENETIDIGIQNHFASREGFG
GIMQMKFCPEYVSVFNNVQENKGASIFNRRGYFSDPALILMHELIHVLHGLYGIKVDDLPI
VPNEKKFFMQSTDTIQAEELYTFGGQDPSIISPSTDKSIYDKVLQNFRGIVDRLNKVLVCISD
PNININIYKNKFKDKYKFVEDSEGKYSIDVESFNKLYKSLMLGFTEINIAENYKIKTRASYFS
DSLPPVKIKNLLDNEIYTIEEGFNISDKNMGKEYRGQNKAINKQ**KNFTGLFEFYKLLCVR**
GIITSK (SEQ ID NO:114)--

Please replace paragraph [00299], beginning on page 74 with the following paragraph:

--In some embodiments, a light chain can be engineered such that one or more segments of the light chain of one or more toxin serotypes replace one or more segments of equal or unequal length within the light chain of another toxin serotype. In a non-limiting example of this kind of chimeric construct, fifty amino acid residues from the N-terminus of the light chain of BoNT/A can replace eight amino acid residues of the N-terminus of the light chain of BoNT/B, resulting in a net gain of fourty-two amino acids in length in the N-terminal region of the light chain chimera. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

M**PFVNKQFNYKDPVNGVDIAYIKIPNAGQMQPVKAFKIHNKIWVIPERDTF**YNDPIDN
DNIIMMEPPFARGTGRYYKAFKITDRIWIIPERYTFGYKPEDFNKSSGIFNRDVCEYYDPDY
LNTNDKKNIFFQTLIKLFNRIKSKPLGEKLLEMIINGIPYLGDRRVPLEEFNTNIASVTVNKLI
SNPGEVERKKGIFANLIIFGPGPVLNENETIDIGIQNHFASREGFGGIMQMKFCPEYVSVFNN

VQENKGASIFNRRGYFSDPALILMHELIHVLHGLYGIKVDDLPIVPNEKKFFMQSTDTIQAE
ELYTFGGQDPSIISPSTDKSIYDKVLQNFRGIVDRLNKVLVCISDPNININIYKNKFKDKYKF
VEDSEGKYSIDVESFNKLYKSLMLGFTEINIAENYKIKTRASYFSDSLPPVKIKNLLDNEIYTI
EEGFNISDKNMGKEYRGQNKAINKQAYEEISKEHLAVYKIQMCKSVK
(SEQ ID NO:116)

Please replace paragraph [00301] beginning on page 75 with the following paragraph:

--In a non-limiting example of this kind of chimeric construct, the last fifty amino acid residues from the C-terminus of the light chain of BoNT/A can replace fifteen amino acid residues within the C-terminus of the light chain of BoNT/E, resulting in a net gain of thirty-five amino acids in the C-terminal region of the light chain chimera. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPKINSFNYNDPVNDRTILYIKPGGCQEFYKSFNIMKNIWIIPERNVIGTTPQDFHPPTSLKN
GDSSYYDPNYLQSDEEKDRFLKIVTKIFNRINNNLSGGILLEELSKANPYLGNDNTPDNQFH
IGDASAVEIKFSNGSQDILLPNVIIMGAEPDLFETNSSNISLRNNYMPSNHGFGSIAIVTFSPE
YSFRFNDNSMNEFIQDPALTLMHELIHSLHGLYGAKGITTKYTITQKQNPLITNIRGTNIEEF
LTFGGTDLNIITSAQSNDIYTNLLADYKKIASKLSKVQVSNPLLNPYKDVFEAKYGLDKDA
SGIYSVNINKFNDIFKKLYSFTEFDLATKFQVKCRQTYIGQYKYFKLSNLLNDSIYNISEGYN
INNLKVNFRGQNANLNPRIITP**GFNLRNTNLAANFNGQNTEINNMNFTKLKNFTGLFEF**
YKLLCVRGIITSKNIVSVKGIRK
(SEQ ID NO:117)--

Please replace paragraph [00303] beginning on page 76 with the following paragraph:

--In a non-limiting example of this kind of chimeric construct, thirty amino acid residues from the N-terminus of the light chain of BoNT/A can replace ten amino acid residues of the N-terminus of the light chain of BoNT/E, resulting in a net gain of twenty amino acids in length in the N-terminal region of the chimera. Additionally, in the same construct, the last fifty amino acid residues from the C-terminus of the light chain of BoNT/A can replace the last fifty amino acid residues from the C-terminus of the light chain of BoNT/E. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPKINSFNY**MPFVNKQFNYKDPVNGVDIAYIKIPNAGQM**YIKPGGCQEFYKSFNIMKNI
WIIPERNVIGTTPQDFHPPTSLKNGDSSYYDPNYLQSDEEKDRFLKIVTKIFNRINNNLSGGI
LLEELSKANPYLGNDNTPDNQFHIGDASAVEIKFSNGSQDILLPNVIIMGAEPDLFETNSSNI
SLRNNYMPSNHGFGSIAIVTFSPEYSFRFNDNSMNEFIQDPALTLMHELIHSLHGLYGAKGI
TTKYTITQKQNPLITNIRGTNIEEFLTFGGTDLNIITSAQSNDIYTNLLADYKKIASKLSKVQV
SNPLLNPYKDVFEAKYGLDKDASGIYSVNINKFNDIFKKLYSFTEFDLATKFQVKCRQTYI
GQYKYFKLSNLLNDSIYNISE**GFNLRNTNLAANFNGQNTEINNMNFTKLKNFTGLFEFY**

KLLCVRGIITSK (SEQ ID NO:118)

Please replace paragraph [00305] beginning on page 76 with the following paragraph:

--In a non-limiting example of this kind of chimeric construct, thirty amino acid residues from the N-terminus of the light chain of BoNT/A can replace ten amino acid residues of the N-terminus of the light chain of BoNT/B, resulting in a net gain of twenty amino acids in length in the N-terminal region of the chimera. Additionally, in the same construct, the last fifty amino acid residues from the C-terminus of the light chain of BoNT/A can replace the last fifty amino acid residues from the C-terminus of the light chain of BoNT/B. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPVTINNFN**MPFVNKQFNYKDPVNGVDIAYIKIPNAGQM**IMMEPPFARGTGRYYKAFKI
TDRIWIIPERYTFGYKPEDFNKSSGIFNRDVCEYYDPDYLNTNDKKNIFFQTLIKLFNRIKSK
PLGEKLLEMIINGIPYLGDRRVPLEEFNTNIASVTVNKLISNPGEVERKKGIFANLIIFGPGPV
LNENETIDIGIQNHFASREGFGGIMQMKFCPEYVSVFNNVQENKGASIFNRRGYFSDPALIL
MHELIHVLHGLYGIKVDDLPIVPNEKKFFMQSTDTIQAEELYTFGGQDPSIISPSTDKSIYDK
VLQNFRGIVDRLNKVLVCISDPNININIYKNKFKDKYKFVEDSEGKYSIDVESFNKLYKSLM
LGFTEINIAENYKIKTRASYFSDSLPPVKIKNLLDNEI**GFNLRNTNLAANFNGQNTEINNM**
NFTKLKNFTGLFEFYKLLCVRGIITSK (SEQ ID NO:119)--

Please replace paragraph [00307] beginning on page 77 with the following paragraph:

--In a non-limiting example of this kind of chimeric construct, thirty amino acid residues from the N-terminus of the light chain of BoNT/A can replace ten amino acid residues of the N-terminus of the light chain of BoNT/F, resulting in a net gain of twenty amino acids in length in the N-terminal region of the chimera. Additionally, in the same construct, the last fifty amino acid residues from the C-terminus of the light chain of BoNT/A can replace the last fifty amino acid residues from the C-terminus of the light chain of BoNT/F. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPVAINSFN**MPFVNKQFNYKDPVNGVDIAYIKIPNAGQM**LYMQIPYEEKSKKYYKAFEI
MRNVWIIPERNTIGTNPSDFDPPASLKNGSSAYYDPNYLTTDAEKDRYLKTTIKLFKRINSN
PAGKVLLQEISYAKPYLGNDHTPIDEFSPVTRTTSVNIKLSTNVESSMLLNLLVLGAGPDIFE
SCCYPVRKLIDPDVVYDPSNYGFGSINIVTFSPEYEYTFNDISGGHNSSTESFIADPAISLAHE
LIHALHGLYGARGVTYEETIEVKQAPLMIAEKPIRLEEFLTFGGQDLNIITSAMKEKIYNNLL
ANYEKIATRLSEVNSAPPEYDINEYKDYFQWKYGLDKNADGSYTVNENKFNEIYKKLYSF
TESDLANKFKVKCRNTYFIKYEFLKVPNLLDDDIY**GFNLRNTNLAANFNGQNTEINNMN**

FTKLKNFTGLFEFYKLLCVRGIITSK (SEQ ID NO:120)--

Please replace paragraph [00309] beginning on page 78 with the following paragraph:

--In some embodiments, the swapped sequences can be derived from two different serotypes, resulting in a chimera with regions from three different serotypes in all. In this example, eight amino acid residues from the N-terminus of the light chain of BoNT/B can replace five amino acid residues of the N-terminus of the light chain of BoNT/E, resulting in a net gain of three amino acids in length in the N-terminal region of the chimera. Additionally, in the same construct, 30 amino acid residues including the dileucine repeat of the C-terminus of the light chain of BoNT/A can replace ten amino acid residues within the C-terminus of the light chain of BoNT/E, resulting in a net gain of 20 amino acids in the C-terminal region of the chimera. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPKINSFNYNDP***VTINNFNY***DRTILYIKPGGCQEFYKSFNIMKNIWIIPERNVIGTTPQDFHP
PTSLKNGDSSYYDPNYLQSDEEKDRFLKIVTKIFNRINNNLSGGILLEELSKANPYLGNDNT
PDNQFHIGDASAVEIKFSNGSQDILLPNVIIMGAEPDLFETNSSNISLRNNYMPSNHGFGSIAI
VTFSPEYSFRFNDNSMNEFIQDPALTLMHELIHSLHGLYGAKGITTKYTITQKQNPLITNIRG
TNIEEFLTFGGTDLNIITSAQSNDIYTNLLADYKKIASKLSKVQVSNPLLNPYKDVFEAKYG
LDKDASGIYSVNINKFNDIFKKLYSFTEFDLATKFQVKCRQTYIGQYKYFKLSNLLNDSIYN
ISEGYNINNLKVNFRGQNANLNPRIITPITGRGLVKKIIRFCK**NNMNFTKLKNFTGLFEFY**
KLLCVRGIITSK

(SEQ ID NO:121)--

Please replace paragraph [00311] beginning on page 78 with the following paragraph:

--In a non-limiting example, eight amino acid residues from the N-terminus of the light chain of BoNT/B can replace five amino acid residues of the N-terminus of the light chain of BoNT/F, resulting in a net gain of three amino acids in length in the N-terminal region of the chimera. Additionally, in the same construct, 30 amino acid residues including the dileucine repeat of the C-terminus of the light chain of BoNT/A can replace ten amino acid residues within the C-terminus of the light chain of BoNT/F, resulting in a net gain of 20 amino acids in the C-terminal region of the chimera. The amino acid sequence of the entire light chain of such a chimeric construct is shown below:

MPVAINSFNYND*VTINNFNY*TILYMQIPYEEKSKKYYKAFEIMRNVWIIPERNTIGTNPSDF
DPPASLKNGSSAYYDPNYLTTDAEKDRYLKTTIKLFKRINSNPAGKVLLQEISYAKPYLGN
DHTPIDEFSPVTRTTSVNIKLSTNVESSMLLNLLVLGAGPDIFESCCYPVRKLIDPDVVYDPS
NYGFGSINIVTFSPEYEYTFNDISGGHNSSTESFIADPAISLAHELIHALHGLYGARGVTYEE
TIEVKQAPLMIAEKPIRLEEFLTFGGQDLNIITSAMKEKIYNNLLANYEKIATRLSEVNSAPP
EYDINEYKDYFQWKYGLDKNADGSYTVNENKFNEIYKKLYSFTESDLANKFKVKCRNTY
FIKYEFLKVPNLLDDDIYTVSEGFNIGNLAVNNRGQSIKLNPKIIDSIPDKGLVEK**NNMNFT**
KLKNFTGLFEFYKLLCVRGIITSKRK (SEQ ID NO:122)--